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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/072,956	05/05/98	CHOREV M	BPC073

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JOHN D CONWAY
BIOMEASURE INC
27 MAPLE STREET
MILFORD MA 01757-3650

EXAMINER	
RUSSEL, J	

ART UNIT	PAPER NUMBER
1654	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/072,956	M. Chorev et al
Examiner	**Group Art Unit**
J. Russel	1654

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 3-3-1999.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-47 is/are pending in the application.

Of the above claim(s)____ is/are withdrawn from consideration.

☐ Claim(s)____ is/are allowed.

☒ Claim(s) 1-10,13,14,16,17,20,21,23,24,27,28,30-32,35,36,38-40,43,44,46,and 47 is/are rejected.

☒ Claim(s) 11,12,15,18,19,22,25,26,29,33,34,37,41,42, and 45 is/are objected to.

☐ Claim(s)____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 8

☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other____

Office Action Summary

1. Claims 13, 14, 20, 21, 27, 28, 35, 36, 43, and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. At claim 13, page 4 of the amendment filed March 3, 1999, line 19, and claim 14, page 6 of the amendment filed March 3, 1999, line 27, "or" should be changed to --and-- so that standard Markush terminology is used. There is no antecedent basis in the claims for the phrase "the compound" at claim 13, page 4 of the amendment filed March 3, 1999, line 27. It is suggested that "compound" be changed to --analogue--.

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1-3, 7, 9, and 13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 5,723,577. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '577 patent anticipate the instant claims. Because of the similarity in structure between the claimed peptides of the '577 patent and Applicants' claimed analogues,

inherently the claimed peptides of the '577 patent will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to the same extent claimed by Applicants.

4. Claims 1-3, 7, 9, 10, and 13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 5,717,062. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '062 patent anticipate the instant claims. Note that the '062 patent claims analogues in which A_{12} can be D-Ala. Because of the similarity in structure between the claimed peptides of the '062 patent and Applicants' claimed analogues, inherently the claimed peptides of the '062 patent will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to the same extent claimed by Applicants.

5. Claims 1-3, 7, 9, and 13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 32 of copending Application No. 08/779,768. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '768 application anticipate the instant claims. Because of the similarity in structure between the claimed peptides of the '768 application and Applicants' claimed analogues, inherently the claimed peptides of the '768 patent will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to the same extent claimed by Applicants.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. Claims 1-3, 7, 9, and 13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of copending Application No. 08/813,534. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '534 application anticipate the instant claims. Because of the similarity in structure between the claimed peptides of the '534 application and Applicants' claimed analogues, inherently the claimed peptides of the '534 patent will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to the same extent claimed by Applicants.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 1-3, 7, 9, and 13 are rejected under 35 U.S.C. 102(f) and/or (g) as being anticipated by U.S. Patent No. 5,723,577. See the above obviousness-type double patenting rejection. Note that U.S. Patent '577 and the instant application are not currently commonly owned.

9. Claims 1-9, 13, 16, 20, 23, 27, 30, 31, 35, 38, 39, 43, 46, and 47 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 5,723,577. See the above obviousness-type double patenting rejection. In addition, U.S. Patent '577 teaches the peptides in combination with pharmaceutically acceptable carriers and teaches the administration of the peptides to stimulate bone growth in a mammal, i.e. for the treatment of osteoporosis. See, e.g., column 5, lines 8-13 and 23-45. Osteoporosis is a divergence from normal mineral metabolism and homeostasis. Sufficient evidence of similarity between the peptides of the U.S. Patent '577 and Applicants' claimed analogues is deemed to be present to shift the burden to Applicants to provide evidence that their claimed analogues are unobviously different than the peptides of the U.S. Patent '577.

10. Claims 1-3, 7, 9, 10, and 13 are rejected under 35 U.S.C. 102(f) and/or (g) as being anticipated by U.S. Patent No. 5,717,062. See the above obviousness-type double patenting rejection. Note that U.S. Patent '062 and the instant application are not currently commonly owned.

11. Claims 1-10, 13, 16, 17, 20, 23, 24, 27, 30-32, 35, 38-40, 43, 46, and 47 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 5,717,062. See the above obviousness-type double patenting rejection. In addition, U.S. Patent '062 teaches the peptides in combination with pharmaceutically acceptable carriers and teaches the administration of the peptides to stimulate bone growth in a mammal, i.e. for the treatment of osteoporosis. See, e.g., column 4, lines 31-64. Osteoporosis is a divergence from normal mineral metabolism and homeostasis. Sufficient evidence of similarity between the peptides of the U.S. Patent '062 and

Applicants' claimed analogues is deemed to be present to shift the burden to Applicants to provide evidence that their claimed analogues are unobviously different than the peptides of the U.S. Patent '062.

12. Claims 1-3, 7, 9, and 13 are rejected under 35 U.S.C. 102(f) and/or (g) as being anticipated by copending Application No. 08/779,768. See the above provisional obviousness-type double patenting rejection. Note that the '768 application and the instant application are not currently commonly owned.

13. Claims 1-9, 13, 16, 20, 23, 27, 30, 31, 35, 38, 39, 43, 46, and 47 are provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 08/779,768 which has a common inventor with the instant application. See the above provisional obviousness-type double patenting rejection. Further, the '768 application teaches in its specification that its peptides can be combined with pharmaceutically acceptable carriers and administered to stimulate bone growth in a mammal, i.e. for the treatment of osteoporosis. See, e.g., page 12, line 30 - page 14, line 12. Osteoporosis is a divergence from normal mineral metabolism and homeostasis. Sufficient evidence of similarity between the peptides of the '768 application and Applicants' claimed analogues is deemed to be present to shift the burden to Applicants to provide evidence that their claimed analogues are unobviously different than the peptides of the '768 application.

Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e), if patented. This provisional rejection under 35 U.S.C. 102(e) is based upon a presumption of future patenting of the copending application.

This provisional rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

This rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

14. Claims 1-3, 7, 9, and 13 are rejected under 35 U.S.C. 102(f) and/or (g) as being anticipated by copending Application No. 08/813,534. See the above provisional obviousness-type double patenting rejection. Note that the '534 application and the instant application are not currently commonly owned.

15. Claims 1-9, 13, 16, 20, 23, 27, 30, 31, 35, 38, 39, 43, 46, and 47 are provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 08/813,534 which has a common inventor with the instant application. See the above provisional obviousness-type double patenting rejection. Further, the '534 application teaches in its specification that its peptides can be combined with pharmaceutically acceptable carriers and administered to stimulate bone growth in a mammal, i.e. for the treatment of osteoporosis. See, e.g., page 10, line 16 - page 11, line 31. Osteoporosis is a divergence from normal mineral metabolism and homeostasis. Sufficient evidence of similarity between the peptides of the '534 application and Applicants' claimed analogues is deemed to be present to shift the burden to Applicants to provide evidence that their claimed analogues are unobviously different than the peptides of the '534 application.

Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e), if patented. This provisional rejection under 35 U.S.C. 102(e) is based upon a presumption of future patenting of the copending application.

This provisional rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

This rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

16. Claims 1-3, 7, 9, 10, 23, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Holick. Holick teaches the peptides [$Nle^{8,18}$, Tyr^{34}]-bpth(1-34)-NH_2, [$Nle^{8,18}$, Tyr^{34}]-hpth(1-34)-NH_2, [$Nle^{8,21}$, Tyr^{34}]-rpth(1-34)-NH_2, bpth(3-34), [$Nle^{8,18}$, Tyr^{34}]-bpth(3-34)-NH_2, [$Nle^{8,18}$, Tyr^{34}]-bpth(7-34)-NH_2, and [Tyr^{34}]-bpth-NH_2, hpth(13-34) which have the same structure recited in formulas (I) and (II). See column 7. The peptides are combined with pharmaceutically acceptable carriers. See column 12, line 65 - column 13, line 13. Because of the similarity in structure between the peptides of Holick and Applicants' claimed analogues, inherently the peptides of Holick will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to the same extent claimed by Applicants. Sufficient evidence of similarity between the peptides of Holick and Applicants' claimed analogues is deemed to be present to shift the burden

to Applicants to provide evidence that their claimed analogues are unobviously different than the peptides of Holick.

17. Claims 1-9, 16, 23, 30, 31, 38, 39, 46, and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Willick et al. Willick et al teaches the PTH analogues from hPTH(1-29)-NH_2 through hPTH(1-31)-NH_2 and from [Leu^{27}]hPTH(1-29)-NH_2 through [Leu^{27}]hPTH(1-31)-NH_2. The analogues are administered in combination with carriers to mammals or humans in need of treatment for osteoporosis, other bone related diseases, and disorders involving bone cell calcium regulation. See, e.g., column 2, lines 43-45 and 53-55, and column 6, lines 40-65. Because of the similarity in structure and effects between the peptides of Willick et al and Applicants' claimed analogues, inherently the peptides of Willick et al will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to the same extent claimed by Applicants. Sufficient evidence of similarity between the peptides of Willick et al and Applicants' claimed analogues is deemed to be present to shift the burden to Applicants to provide evidence that their claimed analogues are unobviously different than the peptides of Willick et al.

18. Claims 1-9, 16, 23, 30, 31, 38, 39, 46, and 47 are rejected under 35 U.S.C. 102(e) as being anticipated by Duvos et al. Duvos et al teach the PTH analogues containing the core sequence hPTH(3-35) and which can optionally be extended on the N-terminus by one or two amino acids and can optionally be extended on the C-terminus by one amino acid. Duvos et al also teaches the hPTH analogues from hPTH(1-34) to hPTH(1-38). The PTH analogues can be combined with an isotonic solution for administration and can be used to regulate the calcium

level in the body and the incorporation of calcium into the bones, and can be used to treat osteoporosis. See, e.g., column 1, lines 54-65; column 2, lines 11-22; column 3, lines 39-59; Table 1; and Tables 6a and 6b. Because of the similarity in structure and effects between the peptides of Duvos et al and Applicants' claimed analogues, inherently the peptides of Duvos et al will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to the same extent claimed by Applicants. Sufficient evidence of similarity between the peptides of Duvos et al and Applicants' claimed analogues is deemed to be present to shift the burden to Applicants to provide evidence that their claimed analogues are unobviously different than the peptides of Duvos et al. Note also that claims 1-6, 46, and 47 do not exclude PTH(1-34)R^3 through PTH(1-38)R^3 as does, e.g., claim 7.

19. Claims 1-6, 46, and 47 are rejected under 35 U.S.C. 102(e) as being anticipated by Duvos et al as applied against claims 1-9, 16, 23, 30, 31, 38, 39, 46, and 47 above, and further in view of Applicants' admission of the prior art at page 1, lines 13-15. With respect to Duvos et al's disclosure of hPTH(1-34), Applicants admit at page 1, lines 13-15, of the specification that hPTH(1-34) is known to selectively activate the PTH2 receptor, and accordingly Applicants' admission is further evidence that Duvos et al anticipates Applicants' claims 1-6, 46, and 47.

20. Claims 1-3, 7, 9, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by the Neugebauer et al article. The Neugebauer et al article teaches the amidated hPTH fragment consisting of residues 20-34. Because of the similarity in structure and effects between the fragment of the Neugebauer et al article and Applicants' claimed analogues, inherently the

fragment of the Neugebauer et al article will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to the same extent claimed by Applicants. Sufficient evidence of similarity between the fragment of the Neugebauer et al article and Applicants' claimed analogues is deemed to be present to shift the burden to Applicants to provide evidence that their claimed analogues are unobviously different than the fragment of the Neugebauer et al article.

21. Claims 1-8, 13, 14, 20, 21, 27, 28, 30, 35, 36, 38, 43, 44, 46, and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Chorev et al '779. Chorev et al '779 teach hHCF (i.e. hPTHrP) analogues having the same structures as set forth in Applicants' formulas I, IV, and V. See, e.g., the analogues set forth at column 3, lines 25-26 and 35-56, and Example 3. The analogues can be combined with a pharmaceutically acceptable carrier and used to treat osteoporosis or hypercalcemia (which are divergences from normal mineral metabolism and homeostasis) and hyperparathyroidism expressed as hypertension (which is abnormal blood pressure). See, e.g., column 4, lines 5-36. Because of the similarity in structure and effects between the peptides of Chorev et al '779 and Applicants' claimed analogues, inherently the peptides of Chorev et al '779 will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to the same extent claimed by Applicants. Sufficient evidence of similarity between the peptides of Chorev et al '779 and Applicants' claimed analogues is deemed to be present to shift the burden to Applicants to provide evidence that their claimed analogues are unobviously different than the peptides of Chorev et al '779.

22. Claims 1-10, 16, 17, 23, 24, 30-32, 38-40, 46, and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakagawa et al. Nakagawa et al teach hPTH analogues which have the same structure as Applicants' formulas I, II, and III. See, e.g., column 6, lines 8-32. The analogues are combined with pharmaceutically acceptable carriers and administered for the treatment of osteoporosis (which is a divergence from normal mineral metabolism and homeostasis) and hypertension (which is abnormal blood pressure). See, e.g., column 3, lines 44-68. Because of the similarity in structure and effects between the peptides of Nakagawa et al and Applicants' claimed analogues, inherently the peptides of Nakagawa et al will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to the same extent claimed by Applicants. Sufficient evidence of similarity between the peptides of Nakagawa et al and Applicants' claimed analogues is deemed to be present to shift the burden to Applicants to provide evidence that their claimed analogues are unobviously different than the peptides of Nakagawa et al.

23. Claims 1-10, 13, 16, 17, 20, 23, 24, 27, 30-32, 35, 38-40, 43, 46, and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application '193. The WO Patent Application '193 teaches analogues of PTH and PTHrP which have the same structure as Applicants' formula I, II, III, and IV. See, e.g., pages 2-5. Note also that the WO Patent Application '193 teaches PTH analogues in which A_{12} can be D-Ala. The WO Patent Application '193 teaches the peptides in combination with pharmaceutically acceptable carriers and teaches the administration of the peptides to stimulate bone growth in a mammal, i.e. for the treatment of

osteoporosis. See, e.g., page 6, line 30 - page 8, line 19. Osteoporosis is a divergence from normal mineral metabolism and homeostasis. Because of the similarity in structure and effect between the analogues of the WO Patent Application '193 and Applicants' claimed analogues, inherently the analogues of the WO Patent Application '193 will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to the same extent claimed by Applicants. Sufficient evidence of similarity between the analogues of the WO Patent Application '193 and Applicants' claimed analogues is deemed to be present to shift the burden to Applicants to provide evidence that their claimed analogues are unobviously different than the analogues of the WO Patent Application '193.

24. Claims 1-3, 7, 9, 10, 13, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by the Chorev et al article. The Chorev et al article teaches analogues of PTH and PTHrP which have the same structures as Applicants' formulas I-V. See, e.g., Table II. Because of the similarity in structure between the peptides of the Chorev et al article and Applicants' claimed analogues, inherently the peptides of the Chorev et al article will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to the same extent claimed by Applicants. Sufficient evidence of similarity between the peptides of the Chorev et al article and Applicants' claimed analogues is deemed to be present to shift the burden to Applicants to provide evidence that their claimed analogues are unobviously different than the peptides of the Chorev et al article.

25. Claims 4-6, 8, 16, 17, 20, 21, 23, 24, 27, 28, 30-32, 35, 36, 38-40, 43, 44, 46, and 47 are rejected under 35 U.S.C. 103(a) as being obvious over the Chorev et al article. Application of the

Chorev et al article is the same as in the above rejection of claims 1-3, 7, 9, 10, 13, and 14. The Chorev et al article establishes that its analogues have agonist, partial agonist, and/or antagonist activities, but does not teach their combination with pharmaceutically acceptable carriers and their administration in vivo. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to combine the analogues of the Chorev et al article with pharmaceutically acceptable carriers and to administer them in vivo to treat diseases which are typically treated with other PTH and PTHrP analogues, including abnormal calcium metabolism and homeostasis, because the Chorev et al article's disclosure of in vitro activity for the analogues is reasonably predictive of in vivo operability, because it is desirable to treat such diseases in vivo, and because therapeutic agents administered in vivo are routinely combined with pharmaceutically acceptable carriers for ease of storage, handling, measurement, and administration.

26. Claims 1-10, 16, 17, 23, 24, 30-32, 38-40, 46, and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Rosenblatt et al '223. Rosenblatt et al '223 teaches parathyroid hormone analogues including [D-Phe^{7},Tyr^{34}]hPTH(7-34)NH_2. The analogues can be combined with pharmaceutically acceptable carriers and administered for the treatment of osteoporosis or hypercalcemia (which are divergences from normal mineral metabolism and homeostasis) and hypertension (which is abnormal blood pressure). See, e.g., column 2, lines 37-43, and column 5, line 18 - column 6, line 8. Because of the similarity in structure and effects between the analogues of Rosenblatt et al '223 and Applicants' claimed analogues, inherently the analogues of Rosenblatt et al '223 will selectively bind to the PTH2 receptor and will agonize or antagonize the receptor to

the same extent claimed by Applicants. Sufficient evidence of similarity between the analogues of Rosenblatt et al '223 and Applicants' claimed analogues is deemed to be present to shift the burden to Applicants to provide evidence that their claimed analogues are unobviously different than the analogues of Rosenblatt et al '223.

27. Claims 1-3, 7, 9, 10, 13, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by the Gardella et al article (J. Biol. Chem., Vol. 271, pages 19888-19893). The Gardella et al article teaches peptides which are selective for the PTH-2 receptor. See the first, third through fifth, ninth through eleventh, and fourteenth through seventeenth peptides listed in Table I.

28. Claims 1-10, 13, 14, 16, 17, 20, 21, 23, 24, 27, 28, 30-32, 35, 36, 38-40, 43, 44, 46, and 47 are rejected under 35 U.S.C. 102(a) as being anticipated by the WO Patent Application '591. The WO Patent Application '591 teaches peptides which are selective for the PTH-2 receptor. See the first, second, fourth through sixth, ninth through twelfth, fourteenth, sixteenth, and eighteenth peptides of Table 1. The peptides are administered therapeutically to treat medical disorders resulting from altered or excessive action of the PTH-2 receptor or to treat osteoporosis. See, e.g., page 27, line 1 - page 28, line 2, and the claims.

29. Applicant's arguments filed March 3, 1999 have been fully considered but they are not persuasive.

Concerning Applicants' paragraph 5, the examiner agrees that the claimed subject matter is defined not only by structure but also by function, and that Applicants have taught how to synthesize and test the compounds of the instant application. However, the examiner does not

agree that "a compound of the instant application has to be synthesized and have tested positive for selective binding to the PTH2 receptor for the compound to fall within the claims of the instant application" (sentence bridging pages 9 and 10 of the response). Actual reduction to practice is not required either for Applicants (it is unlikely that Applicants have actually reduced to practice all of the species encompassed by their claims) or for the prior art (see In re Donohue, 226 USPQ 619, 621 (Fed. Cir. 1985)). Further, the prior art need not teach or suggest the functional limitation, because Applicants are not claiming a functional limitation. Rather, Applicants are claiming compounds, compositions, and methods, and what must be taught or suggested by the prior art is Applicants' claimed compounds, compositions, and methods. Patentability is not established merely upon the employment of descriptive language not chosen by the prior art. In re Skonner, 186 USPQ 80, 82 (CCPA 1975).

Applicants state that "mere similarity of structure is not a basis for assuming that a PTH1 receptor binding compound would selectively bind to the PTH2 receptor" (page 11 of the response, lines 7-9). The examiner disagrees. As a matter of patent law, mere similarity of structure is sufficient to establish prima facie anticipation or obviousness, with the result that the burden shifts to Applicants to provide evidence that the prior art products do not possess the function recited in Applicants' claims. See In re Best, 195 USPQ 430, 433 (CCPA 1977) and MPEP 2112.01. Applicants have not provided evidence that the prior art PTH analogs which satisfy the structural requirements set forth in Applicants' claims do not satisfy the functional requirements set forth in Applicants' claims.

Applicants refer to page 2, line 21 - page 3, line 9, of the specification for a discussion of selective binding and the PTH2 receptor. However, while this section of the specification does explain that there is a difference between binding and selective binding, neither this section of the specification nor any other section provides an explicit definition of selective binding. No comparative binding experiments are reported in the specification which can be used to determine what Applicants mean by "selective" binding. In the absence of such an explicit definition, it is appropriate to rely upon standard definitions of "selective". The ordinary meaning of "selective" would be that a ligand would preferentially bind to the PTH2 receptor rather than to the PTH1 receptor. "Selective" is not a synonym for "exclusive", and a ligand could bind to the PTH1 receptor while still selectively binding to the PTH2 receptor as long as the ligand's affinity for the PTH2 receptor was stronger than the ligand's affinity for the PTH1 receptor. This ordinary meaning of "selective" is supported by Applicants' specification, in particular by page 1, lines 13-15, and page 2, lines 31-32, which describe PTH(1-34) as a selective ligand for the PTH2 receptor, and by page 2, lines 30-31, which acknowledges that PTH(1-34) also binds to the PTH1 receptor.

To the extent that page 2, line 21 - page 3, line 9, distinguishes selective binding from ordinary binding, it implies that Ile^5 and Trp^{23} are necessary for selective binding to the PTH2 receptor (see page 2, line 33 - page 3, line 9), although it is noted that not all of Applicants' claims require these two residues to be present. Many of the PTH analogues taught by the applied

references comprise Ile^5 and Trp^{23}, and thus even in light of Applicants' discussion of selectivity in the specification would have been expected to be selective ligands.

Concerning the '577 patent, the examiner agrees that the reference is applied against Applicants' claims on the basis of the doctrine of inherency. However, it should be noted that where Applicants' claims encompass compounds of the '577 patent, the relationship is Applicants' genus to the '577 patent's species, and a species does anticipate a genus. For example, the genus of claim 1 of the '577 patent is entirely encompassed within the larger generic formula of Applicants' claim 9, and therefore it is proper to argue inherency and prima facie anticipation. Alternatively, the species $[Cha^{7,11}]hPTH(1\text{-}34)NH_2$ at claim 5 of the '577 patent is a species which prima facie anticipates Applicants' genus, and there is no "sub-genus" of this or other single species of the '577 patent. The peptides of the '577 patent have the same structure as is recited in Applicants' claims, and contain Ile^5 and Trp^{23}. As discussed above, the mere fact of binding to the PTH1 receptor is not inconsistent with a peptide being a selective ligand for the PTH2 receptor. Sufficient evidence of similarity is present to establish prima facie anticipation in accordance with Best. Applicants have not met their burden of showing that the peptides of the '577 patent do not possess Applicants' claimed function. Further, the claims of the '577 patent are not limited to analogues which bind the PTH1 receptor. Given the vast number of species encompassed by the generic formulas recited in both the '577 patent and the instant claims, issuance of a second patent encompassing the same species would raise a significant risk of undue extension of the patent

monopoly, and therefore addressing this issue through an obviousness-type double patenting issue is appropriate.

Concerning the obviousness-type double patenting rejection over the '062 patent, the examiner incorporates herein the arguments set forth above with respect to Applicants' paragraph 5. None of the rejected claims contain any limitation which would exclude the presence of a disulfide bond or an amide bond. Silence in the rejected claims does not distinguish over this additional feature present in the compounds of the '062 patent.

Concerning the provisional obviousness-type double patenting rejections over the '768 application and the '534 application, the examiner incorporates herein the arguments set forth above with respect to Applicants' paragraph 5.

Concerning Applicants' paragraph 10, the examiner incorporates herein the arguments et forth above with respect to Applicants' paragraph 5. The examiner agrees that an anticipatory prior art reference must show each claim limitation. However, this does not mean that the prior art reference must use the same descriptive terminology used by Applicants. See Skonner, cited above. If Applicants' argument were to be followed, then an inherency rejection could never be made because by definition, an inherency rejection involves a reference which does not describe a function or characteristic or result which is recited in a claim. Because inherency rejections are accepted under the patent law, Applicant's argument can not be accepted. For compound claims, an anticipatory prior art reference needs to teach the compound, but does not need to teach all the

properties of the compound which Applicants choose to describe the compound. Prima facie, the '577 patent teaches Applicants' compounds.

As discussed above, Applicants do not define in their specification that "selective" means no binding to the PTH1 receptor occurs. This definition of "selective" set forth in the arguments contradicts Applicants' use of the term in the specification, where PTH-(1-34) is described as a selective ligand for the PTH2 receptor but also is described as binding to the PTH1 receptor. To the extent that the arguments contradict the specification, the latter is controlling. Further, there is no evidence of record, either in the instant application or in the '577 patent, that the exemplified compounds of the '577 patent selectively bind to the PTH1 receptor as alleged in the response. The '577 patent does not describe its peptides as selectively binding to the PTH1 receptor; there is no comparative binding data of record which would permit a conclusion of selective binding for one or the other receptor; and the binding of the peptides of claim 17 of the '577 patent is not tested at all. As discussed above, the relationship between Applicants' claims and the '577 patent is deemed to be Applicants' genus and the '577 patent's species, and a species does anticipate a genus.

The rejection under 35 U.S.C. 102(e) with respect to the '577 patent; the rejections under 35 U.S.C. 102(f) and/or (g) and 35 U.S.C. 102(e) with respect to the '062 patent; the rejections under 35 U.S.C. 192(f) and/or (g) and 35 U.S.C. 102(e) with respect to the '768 application; and the rejections under 35 U.S.C. 192(f) and/or (g) and 35 U.S.C. 102(e) with respect to the '534

application; are maintained for the reasons set forth above with respect to Applicants' paragraphs 5 and 10.

With respect to paragraph 18, the rejection over Holick is maintained for the reasons set forth above in response to Applicants' paragraphs 5 and 10. Structural similarity is sufficient to establish prima facie anticipation under Best. With respect to instant claim 10, the species [$Nle^{8,18}$, Tyr^{34}]-bpth(7-34)-NH_2 and hpth(13-34) of Holick satisfy Applicants' proviso clause. In particular, for these two species, even though A^8 is not a lipophilic D-amino acid, A^6 and A^6, A^7, and A^9-A^{12}, respectively, are deleted.

With respect to paragraph 19, the rejection over Willick et al is maintained for the reasons set forth above in response to Applicants' paragraphs 5 and 10.

With respect to paragraph 20, the rejection over Duvos et al is maintained for the reasons set forth above in response to Applicants' paragraphs 5 and 10.

With respect to paragraph 21, the rejection over Duvos et al is maintained for the reasons set forth above in response to Applicants' paragraphs 5 and 10. With respect to the terminology "PTH analogue", native PTH consists of 84 amino acids. See, e.g., the '577 patent at column 1, lines 13-14; the '062 patent at column 1, lines 5-6; Holick at column 2, lines 20-21, etc. PTH-(1-34) is not the native sequence, but rather is a fragment of the native sequence and therefore is encompassed by Applicants' terminology.

With respect to paragraph 22, the rejection over the Neugebauer et al article is maintained for the reasons set forth above in response to Applicants' paragraphs 5 and 10. With respect to

instant claim 10, the species hpth(20-34)NH_2 of the Neugebauer et al article satisfies Applicants' proviso clause. In particular, for this species, even though A^8 is not a lipophilic D-amino acid, A^6, A^7, and A^9-A^{19} , respectively, are deleted.

With respect to paragraph 23, the rejection over Chorev et al '779 is maintained for the reasons set forth above in response to Applicants' paragraphs 5 and 10. Concerning instant claim 14, the claim contains no language which would exclude the Lys^{13}-Asp^{17} bond which occurs inn the species of Chorev et al '779.

With respect to paragraph 24, the rejection over Nakagawa et al is maintained for the reasons set forth above in response to Applicants' paragraphs 5 and 10. With respect to instant claim 10, species 6, 7, and 8 of the Nakagawa et al satisfies Applicants' proviso clause. In particular, for these species, even though A^8 is not a lipophilic D-amino acid, A^{12} is a D-amino acid.

With respect to paragraph 25, the rejection over the WO Patent Application '193 is maintained for the reasons set forth above in response to Applicants' paragraphs 5, 6, and 10.

With respect to paragraph 26, the rejection over the Chorev et al article is maintained for the reasons set forth above in response to Applicants' paragraphs 5 and 10. With respect to instant claims 10 and 14, numerous species of Table II of the Chorev et al article satisfy Applicants' proviso clauses. For example, for the species [D-Ala^{12}, Tyr^{34}]hPTH(1-34)NH_2, even though A^8 is not a lipophilic D-amino acid, A^{12} is a D-amino acid. For the species [Ala^{12}, Tyr^{34}]hPTH(7-34)NH_2, even though A^8 is not a lipophilic D-amino acid, A^6, A^7, and A^9-A^{11} are

deleted. A^{12} of claims 10 and 12 can be D-Ala, D-Trp, or any other D-amino acid because the proviso clause permits this ("when A^8 is not a lipophilic D-amino acid or is not deleted then at least one of... A^{12} is a D-amino acid"). Because D-amino acids are not explicitly recited in the definitions of A^6, A^7, and A^9-A^{12}, the only way for this section of the proviso clause to have meaning is to also permit these residues to be any D-amino acid.

With respect to paragraph 27, the rejection over the Chorev et al article is maintained for the reasons set forth above in response to Applicants' paragraphs 5 and 10. The obviousness rejection concerns the obviousness of using the peptides of the Chorev et al article pharmaceutically, and not of the obviousness of selecting PTH analogs which are selective for the PTH2 receptor.

With respect to paragraph 28, the rejection over Rosenblatt et al '223 is maintained for the reasons set forth above in response to Applicants' paragraphs 5 and 10. With respect to instant claim 10, the peptide of Rosenblatt et al '223 satisfies Applicants' proviso clause. In particular, for this species, even though A^8 is not a lipophilic D-amino acid, A^7 is a D-amino acid and A^6 is deleted.

30. Claims 11, 12, 15, 18, 19, 22, 25, 26, 29, 33, 34, 37, 41, 42, and 45 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

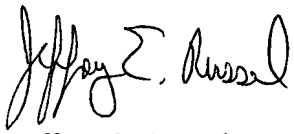
31. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on March 3, 1999 prompted the new ground(s) of rejection

presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (703) 308-0254. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 305-7939 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel
Primary Patent Examiner
Art Unit 1654

JRussel
April 1, 1999